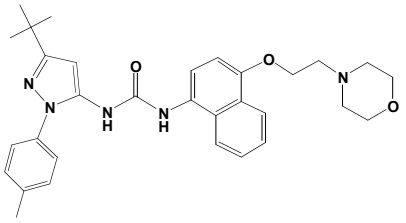
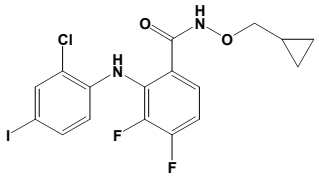
Supplementary Figure S1

BIRB 0796



PD 184352



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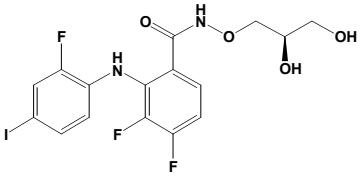

PD 0325901-Cl
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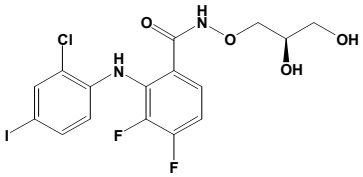

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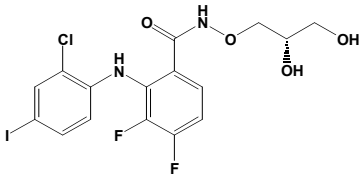

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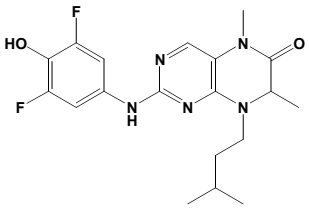

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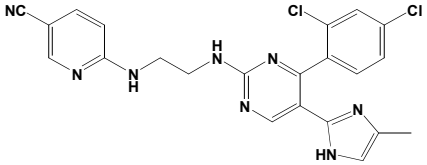

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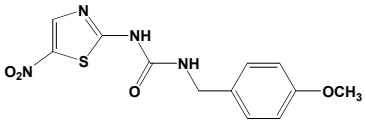

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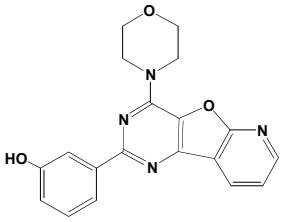

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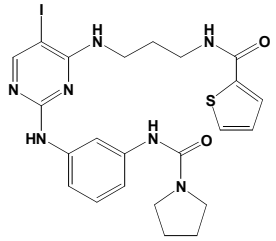
Figure 1 continued

BX795



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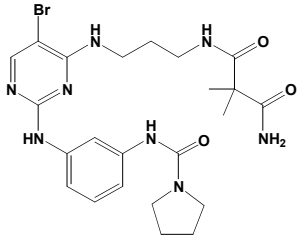

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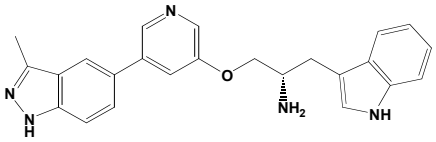

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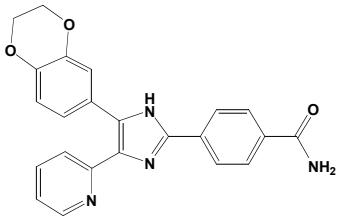

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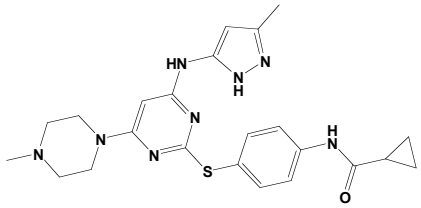

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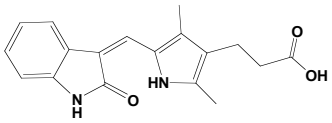

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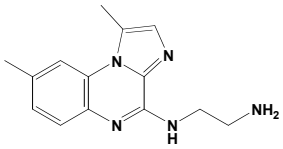

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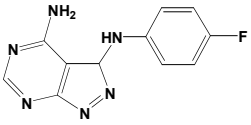

Legend to Figure S1

Figure S1. Structures of the compounds that were synthesised by our laboratory for this study. To our knowledge, the derivative of PD 0325901 in which one of the fluorines is substituted by chlorine has not been named previously and we therefore refer to it here as PD 0325901-Cl.

Table S1 - Abbreviations used in the paper

Protein Kinases.

ALK, activin receptor-like kinase
AMPK, AMP-activated protein kinase;
BRSK, brain specific kinase;
CAMK, calmodulin-dependent kinase;
CAMKK, CAMK kinase;
CDK, cyclin-dependent protein kinase;
CHK, checkpoint kinase;
CK, casein kinase;
CSK, C-terminal Src kinase;
DYRK, dual specificity tyrosine phosphorylated and regulated kinase;
EF2K, elongation factor 2 kinase;
ERK, extracellular signal regulated kinases;
FGFR, fibroblast growth factor receptor
GSK3, glycogen synthase kinase 3;
GAK, cyclin G associated kinase;
HIPK, homeodomain-interacting protein kinase;
IKK, IκB kinase;
JNK, c-Jun N-terminal kinase;
Lck, lymphocyte kinase;
MAPK, mitogen activated protein kinase;
MAPKAP-K, MAPK-activated protein kinase;
MARK, microtubule affinity regulating kinase ;
MELK, maternal embryonic leucine zipper kinase,
MKK1, MAPK kinase-1 (also called MEK1, MAPK or ERK kinase 1);
MNK, MAPK-integrating protein kinase;
MSK, mitogen and stress-activated protein kinase;
MST, mammalian homologue Ste20-like kinase;
NEK, NIMA-related kinase**;**
PAK, p21-activated protein kinase;
PDK1, 3-phosphoinositide dependent protein kinase;
PHK, phosphorylase kinase;
PIM1, provirus integration site for Moloney murine leukaemia virus;
PKA, cyclic AMP dependent protein kinase;
PKB, protein kinase B (also called AKT);
PKC, protein kinase C;
PKD, protein kinase D;
PLK, polo-like kinase;
PRAK, p38-reguated activated kinase;
PRK, Protein Kinase C-related kinase;
RIP2, receptor interacting protein 2;
ROCK, Rho-dependent protein kinase;
RSK, ribosomal S6 kinase;
SGK, serum and glucocorticoid-induced kinase;
SmMLCK, smooth muscle myosin light chain kinase;
Src, sarcoma kinase;
SRPK, serine arginine protein kinase;
TBK1, TANK-binding kinase 1;
YES1, Yamaguchi sarcoma viral oncogene homologue 1

Table S2 The specificities of Bis-indoylmaleimides and isoquinaline sulphonamide derivatives

The concentrations of compounds used in the assays are indicated below each molecule and the results are presented as % activity remaining in the presence of inhibitors as compared to control incubations with inhibitor omitted (averages of duplicate determinations). Each experiment was repeated two or three times with similar results. Further details of the assays are given under experimenta

	LY333531	UCN-01	RO318220	GO6976	KT5720	Rottlerin	H-7	H-8	H-89	HA-1077	H-1152	Y27632
Kinase	0.1 μM	0.01 μM	0.1 μM	0.1 μM	1 μM	10 μM	10 μM	10 μM	1 μM	10 μM	1 μM	10 μM
MKK1	42 ± 6	75 ± 0	87 ± 4	34 ± 4	**16** ± 2	83 ± 5	88 ± 2	66 ± 9	74 ± 7	78 ± 1	77 ± 6	96 ± 1
ERK1	84 ± 5	112 ± 6	88 ± 6	44 ± 6	76 ± 8	92 ± 6	98 ± 3	85 ± 2	90 ± 2	87 ± 6	89 ± 5	98 ± 1
ERK2	94 ± 1	89 ± 4	92 ± 1	41 ± 2	70 ± 7	88 ± 8	84 ± 4	88 ± 6	88 ± 4	91 ± 4	98 ± 4	82 ± 8
JNK1	87 ± 7	79 ± 8	93 ± 3	69 ± 2	48 ± 6	72 ± 7	84 ± 2	87 ± 4	88 ± 3	93 ± 2	97 ± 1	79 ± 8
JNK2	99 ± 0	92 ± 8	92 ± 3	68 ± 0	66 ± 6	107 ± 6	95 ± 3	92 ± 4	98 ± 4	104 ± 2	97 ± 6	90 ± 4
JNK3	112 ± 0	107 ± 0	102 ± 1	79 ± 0	50 ± 1	80 ± 6	84 ± 4	99 ± 0	93 ± 2	105 ± 4	102 ± 0	93 ± 0
p38α MAPK	96 ± 8	105 ± 7	102 ± 3	100 ± 3	91 ± 5	110 ± 4	85 ± 2	103 ± 7	99 ± 1	95 ± 2	100 ± 2	105 ± 4
P38β MAPK	109 ± 2	105 ± 4	99 ± 4	100 ± 3	83 ± 4	109 ± 9	93 ± 5	96 ± 2	91 ± 3	102 ± 6	103 ± 3	109 ± 3
p38γ MAPK	104 ± 5	104 ± 5	98 ± 4	84 ± 7	85 ± 5	97 ± 7	86 ± 1	92 ± 0	102 ± 1	104 ± 5	98 ± 4	102 ± 1
p38δ MAPK	93 ± 3	94 ± 2	92 ± 1	82 ± 1	92 ± 4	86 ± 5	81 ± 2	86 ± 1	98 ± 3	82 ± 8	96 ± 8	87 ± 4
ERK8	92 ± 6	92 ± 3	51 ± 0	38 ± 6	22 ± 4	78 ± 6	79 ± 5	79 ± 5	93 ± 7	71 ± 3	104 ± 0	94 ± 1
RSK1	**10** ± 3	**25** ± 3	**11** ± 5	**6** ± 1	23 ± 2	71 ± 6	**25** ± 1	**26** ± 2	**36** ± 4	**19** ± 2	**22** ± 5	**21** ± 2
RSK2	**12** ± 1	**29** ± 4	**4** ± 2	**5** ± 1	34 ± 5	67 ± 5	**45** ± 5	**45** ± 4	**55** ± 6	**30** ± 0	**39** ± 8	**43** ± 8
PDK1	**25** ± 1	**2** ± 1	62 ± 6	11 ± 1	**4** ± 1	79 ± 3	80 ± 4	80 ± 6	91 ± 6	72 ± 3	57 ± 6	75 ± 1
PKBα	90 ± 7	79 ± 2	52 ± 2	96 ± 1	86 ± 4	88 ± 3	87 ± 4	40 ± 2	**14** ± 1	47 ± 1	92 ± 2	73 ± 2
PKBβ	83 ± 4	77 ± 4	60 ± 1	81 ± 1	96 ± 5	92 ± 5	81 ± 4	64 ± 1	**21** ± 2	75 ± 2	86 ± 3	86 ± 0
SGK1	66 ± 4	83 ± 1	39 ± 4	44 ± 3	35 ± 6	76 ± 8	69 ± 1	65 ± 4	62 ± 0	63 ± 6	82 ± 5	72 ± 4
S6K1	52 ± 5	96 ± 3	20 ± 0	12 ± 0	63 ± 4	69 ± 7	43 ± 4	**35** ± 3	**11** ± 1	28 ± 1	86 ± 7	93 ± 1
PKA	59 ± 2	63 ± 3	51 ± 2	50 ± 4	66 ± 5	69 ± 8	46 ± 1	**15** ± 1	**15** ± 0	**8** ± 1	**31** ± 1	73 ± 1
ROCK 2	94 ± 6	86 ± 4	88 ± 5	53 ± 3	73 ± 7	90 ± 3	**16** ± 1	**13** ± 0	**6** ± 0	**5** ± 0	**3** ± 1	**7** ± 0
PRK2	38 ± 4	**10** ± 3	**8** ± 2	**5** ± 3	**14** ± 2	80 ± 3	**7** ± 2	**7** ± 2	**7** ± 2	**7** ± 1	**15** ± 5	**4** ± 2
PKCα	**4** ± 1	**6** ± 0	**3** ± 0	**2** ± 0	95 ± 5	73 ± 10	60 ± 3	72 ± 3	80 ± 5	58 ± 2	61 ± 5	58 ± 2
PKC ζ	91 ± 7	78 ± 5	25 ± 5	78 ± 4	85 ± 7	104 ± 10	60 ± 4	60 ± 5	55 ± 3	60 ± 2	76 ± 1	55 ± 7
PKD1	91 ± 3	83 ± 5	**66** ± 7	**5** ± 1	**19** ± 5	71 ± 9	**31** ± 3	**28** ± 1	56 ± 4	**21** ± 0	87 ± 4	86 ± 4
MSK1	44 ± 4	68 ± 7	**11** ± 3	**6** ± 1	49 ± 4	82 ± 1	**36** ± 4	**29** ± 2	**9** ± 3	**20** ± 1	**38** ± 5	**27** ± 2
MNK1	94 ± 5	85 ± 1	95 ± 3	67 ± 1	62 ± 4	85 ± 0	65 ± 4	60 ± 1	90 ± 3	**30** ± 2	50 ± 2	**25** ± 3
MNK2	101 ± 2	103 ± 2	103 ± 1	30 ± 1	38 ± 3	90 ± 6	80 ± 3	98 ± 1	97 ± 1	46 ± 3	68 ± 3	55 ± 2
MAPKAP-K2	114 ± 3	75 ± 5	90 ± 7	118 ± 3	43 ± 1	43 ± 7	82 ± 0	115 ± 1	111 ± 8	75 ± 6	93 ± 2	91 ± 2
MAPKAP-K3	90 ± 3	107 ± 4	90 ± 1	95 ± 6	96 ± 8	56 ± 1	98 ± 4	90 ± 6	105 ± 1	102 ± 3	107 ± 1	100 ± 5
PRAK	82 ± 9	83 ± 1	80 ± 9	76 ± 3	83 ± 7	36 ± 9	96 ± 3	63 ± 4	89 ± 5	88 ± 0	96 ± 2	78 ± 3
CAMKKα	97 ± 4	58 ± 3	104 ± 1	27 ± 5	55 ± 3	55 ± 2	85 ± 1	96 ± 5	102 ± 3	95 ± 3	108 ± 1	107 ± 6
CAMKKβ	53 ± 4	**21** ± 0	65 ± 3	**11** ± 4	32 ± 1	50 ± 6	99 ± 4	93 ± 6	102 ± 3	87 ± 1	79 ± 2	75 ± 5
CAMK1	93 ± 1	86 ± 3	91 ± 1	98 ± 4	83 ± 4	86 ± 5	64 ± 7	89 ± 7	101 ± 2	102 ± 3	111 ± 6	98 ± 6
SmMLCK	66 ± 5	83 ± 9	63 ± 1	40 ± 2	55 ± 4	49 ± 9	83 ± 2	82 ± 7	91 ± 7	100 ± 3	86 ± 3	91 ± 7
PHK	49 ± 7	**5** ± 1	46 ± 4	**1** ± 1	**9** ± 4	70 ± 10	72 ± 6	60 ± 2	76 ± 3	52 ± 5	**21** ± 5	50 ± 6
CHK1	71 ± 1	**12** ± 2	59 ± 5	**1** ± 0	**17** ± 2	95 ± 4	90 ± 3	92 ± 6	71 ± 3	90 ± 4	86 ± 0	73 ± 1
CHK2	92 ± 4	96 ± 1	99 ± 5	43 ± 5	47 ± 6	**12** ± 1	90 ± 4	92 ± 2	69 ± 4	66 ± 6	82 ± 1	100 ± 1
GSK3β	43 ± 2	77 ± 5	**4** ± 0	**18** ± 2	73 ± 3	82 ± 7	76 ± 7	59 ± 3	88 ± 3	78 ± 7	92 ± 3	86 ± 3
CDK2-Cyclin A	68 ± 2	44 ± 0	**3** ± 0	**8** ± 0	81 ± 5	93 ± 5	54 ± 3	59 ± 5	75 ± 3	71 ± 0	68 ± 5	51 ± 2
PLK1	85 ± 3	76 ± 7	82 ± 1	80 ± 2	95 ± 3	**24** ± 6	88 ± 2	80 ± 1	95 ± 1	93 ± 1	95 ± 7	85 ± 4
AURORA B	65 ± 2	59 ± 0	80 ± 4	**17** ± 0	**11** ± 1	38 ± 1	78 ± 4	78 ± 8	70 ± 6	63 ± 3	**17** ± 7	80 ± 8
AURORA C	92 ± 5	71 ± 5	77 ± 3	44 ± 6	**21** ± 2	54 ± 3	83 ± 4	77 ± 3	73 ± 4	73 ± 8	**20** ± 5	66 ± 1
AMPK	71 ± 9	**9** ± 1	84 ± 4	50 ± 2	40 ± 5	108 ± 7	67 ± 1	64 ± 2	73 ± 0	76 ± 2	**26** ± 0	**14** ± 1
MARK3	73 ± 2	**6** ± 2	77 ± 5	**12** ± 4	25 ± 2	79 ± 3	93 ± 1	74 ± 7	74 ± 4	76 ± 1	66 ± 4	69 ± 3
BRSK2	67 ± 2	27 ± 6	65 ± 2	46 ± 6	**15** ± 1	92 ± 4	64 ± 2	42 ± 8	82 ± 4	45 ± 4	42 ± 6	57 ± 4
MELK	65 ± 7	53 ± 8	61 ± 4	**15** ± 2	**17** ± 3	70 ± 4	**37** ± 3	**23** ± 1	43 ± 1	**24** ± 1	**34** ± 2	65 ± 1
CK1δ	100 ± 1	96 ± 1	96 ± 7	88 ± 6	93 ± 8	87 ± 4	82 ± 1	83 ± 3	91 ± 6	82 ± 3	95 ± 1	94 ± 4
CK2	89 ± 3	92 ± 3	99 ± 5	88 ± 4	105 ± 6	93 ± 6	89 ± 2	83 ± 5	100 ± 4	97 ± 6	94 ± 5	90 ± 8
DYRK1A	74 ± 1	90 ± 8	31 ± 1	30 ± 6	49 ± 2	82 ± 7	86 ± 8	96 ± 3	96 ± 7	90 ± 4	91 ± 2	81 ± 5
DYRK2	85 ± 1	92 ± 9	90 ± 1	49 ± 5	76 ± 3	87 ± 4	102 ± 5	98 ± 3	105 ± 9	91 ± 4	95 ± 6	86 ± 5
DYRK3	64 ± 5	84 ± 7	55 ± 4	28 ± 3	35 ± 5	39 ± 8	50 ± 2	51 ± 3	65 ± 0	**32** ± 4	108 ± 7	90 ± 9
NEK2a	91 ± 5	85 ± 2	84 ± 1	87 ± 3	87 ± 6	101 ± 3	87 ± 1	89 ± 4	102 ± 7	93 ± 5	94 ± 2	86 ± 5
NEK6	93 ± 1	104 ± 2	97 ± 6	96 ± 6	92 ± 7	92 ± 8	102 ± 8	85 ± 4	104 ± 6	103 ± 8	104 ± 6	92 ± 9
NEK7	104 ± 5	99 ± 0	101 ± 2	98 ± 5	87 ± 3	110 ± 11	93 ± 3	94 ± 3	99 ± 1	111 ± 3	99 ± 4	103 ± 6
IKKβ	86 ± 6	86 ± 1	91 ± 3	76 ± 0	83 ± 3	65 ± 1	86 ± 5	88 ± 5	98 ± 2	95 ± 4	97 ± 4	79 ± 1
PIM1	**4** ± 1	52 ± 2	45 ± 7	20 ± 1	33 ± 4	58 ± 6	99 ± 5	91 ± 5	90 ± 2	83 ± 5	88 ± 3	88 ± 0
PIM2	41 ± 3	73 ± 4	30 ± 1	53 ± 3	62 ± 3	98 ± 4	87 ± 2	96 ± 9	91 ± 7	82 ± 5	88 ± 3	91 ± 2
PIM3	**5** ± 1	**8** ± 1	**16** ± 1	**7** ± 1	**18** ± 1	**14** ± 2	83 ± 0	68 ± 7	91 ± 0	80 ± 2	96 ± 3	56 ± 1
SRPK1	95 ± 2	71 ± 1	82 ± 7	92 ± 6	87 ± 3	**7** ± 1	86 ± 4	92 ± 7	93 ± 5	101 ± 0	99 ± 4	87 ± 6
MST2	37 ± 1	**2** ± 1	80 ± 5	**3** ± 1	44 ± 4	63 ± 6	69 ± 2	50 ± 4	81 ± 6	56 ± 7	66 ± 7	47 ± 4
EF2K	90 ± 1	105 ± 8	101 ± 4	100 ± 6	99 ± 6	84 ± 9	87 ± 4	103 ± 4	102 ± 1	76 ± 7	86 ± 4	85 ± 4
HIPK2	63 ± 1	109 ± 3	88 ± 4	63 ± 3	98 ± 7	77 ± 10	97 ± 4	106 ± 7	101 ± 9	101 ± 6	109 ± 7	83 ± 4
HIPK3	65 ± 6	116 ± 1	78 ± 9	74 ± 2	100 ± 2	86 ± 7	101 ± 1	95 ± 4	106 ± 4	101 ± 5	109 ± 3	98 ± 3
PAK4	75 ± 9	33 ± 1	75 ± 3	**5** ± 0	56 ± 8	37 ± 4	92 ± 5	82 ± 3	82 ± 2	83 ± 3	82 ± 3	90 ± 2
PAK5	79 ± 6	36 ± 0	79 ± 4	**6** ± 0	73 ± 12	75 ± 1	89 ± 7	81 ± 7	84 ± 2	77 ± 1	85 ± 1	90 ± 3
PAK6	81 ± 4	35 ± 1	76 ± 1	**6** ± 0	86 ± 2	94 ± 7	84 ± 5	78 ± 3	76 ± 4	78 ± 4	81 ± 4	88 ± 3
Src	97 ± 1	76 ± 4	91 ± 6	65 ± 2	77 ± 8	80 ± 8	87 ± 5	92 ± 1	100 ± 7	73 ± 5	83 ± 4	80 ± 5
Lck	69 ± 6	50 ± 9	66 ± 3	53 ± 5	80 ± 3	81 ± 10	75 ± 2	72 ± 1	74 ± 6	82 ± 5	69 ± 3	73 ± 4
CSK	78 ± 1	80 ± 0	77 ± 6	75 ± 2	94 ± 5	87 ± 9	85 ± 4	76 ± 1	89 ± 3	72 ± 0	86 ± 7	70 ± 3